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CONTENTS/SUMMARIES

Summary: The cell surface of Candida albicans is composed of a variety of polysaccharides such as glucan, chitin, and mannan. The first two components primarily provide structure, while the mannan, often covalently linked to protein, constitutes the major antigen of the organism. Mannoproteins also have enzymatic activity (acid protease) and ligand-receptor functions. The complement receptors of C. albicans appear to be mannoproteins that are required for the adherence of the organism to endothelial cells. This is certainly true of the CR3-like protein of C. albicans. Proof that the CR3 is the Candida receptor for endothelial cells is derived from two observations. First, mutants lacking CR3 activity are less adherent in vitro and, in fact, less virulent. Second, the ligand recognized by the CR3 receptor (C3bi) as well as anti-CR3 antibodies blocks adherence of the organism to endothelial cells. The CR2 of C. albicans appears to promote the adherence of the organism to plastic substrates. Unlike the CR2 of mammalian cells, the Candida CR2 recognizes ligands containing the RGD sequence of amino acids in addition to the C3d ligand, which does not contain the RGD sequence. There is uncertainty as to whether the Candida CR2 and CR3 are, in fact, different proteins. A mannoprotein has also been described as the adhesin for epithelial cells. In this case, the receptor has a lectinlike activity and recognizes fucose- or glucosamine-containing glycoproteins of epithelial cells, depending on the strain of C. albicans. The oligosaccharide component of the receptor is probably not involved in ligand recognition and may serve to stabilize the receptor. However, the oligosaccharide factor 6 epitope of mannan may also provide adhesin activity in the recognition of epithelial cells. Mannoproteins can be extracted from cells by a number of reagents. Zymolyase, for instance, tends to remove structural mannoproteins, which contain relatively little protein and are linked to glucan. Reagents such as dithiothreitol, on the other hand, tend to extract mannoproteins containing higher amounts of protein that appear to have receptor function. The mannoproteins of C. albicans are dynamically expressed and may be growth phase and growth form specific.

Summary: Lyme disease is a chronic inflammatory disorder resulting from infection by the tick-borne spirochete Borrelia burgdorferi. The pathogenesis of this disease is a complex process resulting from host responses to a limited number of organisms. Once introduced into the skin at the site of a tick bite, the spirochetes disseminate to distant locations. This step involves adherence to and penetration across endothelium, a process which has been observed in vitro. The organism's ability to adhere to different

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eucaryotic cell types in vitro and the wide distribution of the spirochete in infected humans and experimentally infected animals lead to the conclusion that B. burgdorferi can invade successfully and remain associated with many different organs. While phagocytosis and complement activation have been observed in vitro, the specific immune response that develops in humans is inefficient in eradicating the organisms, which may possess some mechanism(s) to evade this response. There is significant evidence for host autoreactivity based on antigenic cross-reactivity between proteins of the organism and endogenous host cell components. The study of the pathogen-host interactions in this disease should increase our understanding of this chronic bacterial infection, provide insight into vaccine protocols, and improve therapeutic approaches.

Summary: The current model of cellulose biogenesis in plants, as well as bacteria, holds that the membranous cellulose synthase complex polymerizes glucose moieties from UDP-Glc into β-1,4-glucan chains which give rise to rigid crystalline fibrils upon extrusion at the outer surface of the cell. The distinct arrangement and degree of association of the polymerizing enzyme units presumably govern extracellular chain assembly in addition to the pattern and width of cellulose fibril deposition. Most evident for Acetobacter xylinum, polymerization and assembly appear to be tightly coupled. To date, only bacteria have been effectively studied at the biochemical and genetic levels. In A. xylinum, the cellulose synthase, composed of at least two structurally similar but functionally distinct subunits, is subject to a multicomponent regulatory system. Regulation is based on the novel nucleotide cyclic diguanylic acid, a positive allosteric effector, and the regulatory enzymes maintaining its intracellular turnover: diguanylate cyclase and Ca^{2+}-sensitive bis-(3',5')-cyclic diguanylic acid (c-di-GMP) phosphodiesterase. Four genes have been isolated from A. xylinum which constitute the operon for cellulose synthesis. The second gene encodes the catalytic subunit of cellulose synthase; the functions of the other three gene products are still unknown. Exclusively an extracellular product, bacterial cellulose appears to fulfill diverse biological roles within the natural habitat, conferring mechanical, chemical, and physiological protection in A. xylinum and Sarcina ventriculi or facilitating cell adhesion during symbiotic or infectious interactions in Rhizobium and Agrobacterium species. A. xylinum is proving to be most amenable for industrial purposes, allowing the unique features of bacterial cellulose to be exploited for novel product applications.

Summary: In this review we discuss the degradation of chlorinated hydrocarbons by microorganisms, emphasizing the physiological, biochemical, and genetic basis of the biodegradation of aliphatic, aromatic, and polycyclic compounds. Many environmentally important xenobiotics are halogenated, especially chlorinated. These compounds are manufactured and used as pesticides, plasticizers, paint and printing-ink components, adhesives, flame retardants, hydraulic and heat transfer fluids, refrigerants, solvents, additives for cutting oils, and textile auxiliaries. The hazardous chemicals enter the environment through production, commercial application, and waste. As a result of bioaccumulation in the food chain and groundwater contamination, they pose public health problems because many of them are toxic, mutagenic, or carcinogenic. Although synthetic chemicals are usually recalcitrant to biodegradation, microorganisms have evolved an extensive range of enzymes, pathways, and control mechanisms that are responsible for catabolism of a wide variety of such compounds. Thus, such biological degradation can be exploited to alleviate environmental pollution problems. The pathways by which a given compound is degraded are determined by the physical, chemical, and microbiological aspects of a particular environment. By understanding the genetic basis of catabolism of xenobiotics, it is possible to improve the efficacy of naturally occurring microorganisms or construct new microorganisms capable of degrading pollutants in soil and aquatic environments more efficiently. Recently a number of genes whose enzyme products have a broader substrate specificity for the degradation of aromatic compounds have been cloned and attempts have been made to

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construct gene cassettes or synthetic operons comprising these degradative genes. Such gene cassettes or operons can be transferred into suitable microbial hosts for extending and custom designing the pathways for rapid degradation of recalcitrant compounds. Recent developments in designing recombinant microorganisms and hybrid metabolic pathways are discussed.

Summary: Poxviruses are a highly successful family of pathogens, with variola virus, the causative agent of smallpox, being the most notable member. Poxviruses are unique among animal viruses in several respects. First, owing to the cytoplasmic site of virus replication, the virus encodes many enzymes required either for macromolecular precursor pool regulation or for biosynthetic processes. Second, these viruses have a very complex morphogenesis, which involves the de novo synthesis of virus-specific membranes and inclusion bodies. Third, and perhaps most surprising of all, the genomes of these viruses encode many proteins which interact with host processes at both the cellular and systemic levels. For example, a viral homolog of epidermal growth factor is active in vaccinia virus infections of cultured cells, rabbits, and mice. At least five virus proteins with homology to the serine protease inhibitor family have been identified and one, a 38-kDa protein encoded by cowpox virus, is thought to block a host pathway for generating a chemotactic substance. Finally, a protein which has homology with complement components interferes with the activation of the classical complement pathway. Poxviruses infect their hosts by all possible routes: through the skin by mechanical means (e.g., molluscum contagiosum infections of humans), via the respiratory tract (e.g., variola virus infections of humans), or by the oral route (e.g., ectromelia virus infection of the mouse). Poxvirus infections, in general, are acute, with no strong evidence for latent, persistent, or chronic infections. They can be localized or systemic. Ectromelia virus infection of the laboratory mouse can be systemic but inapparent with no mortality and little morbidity, or highly lethal with death in 10 days. On the other hand, molluscum contagiosum virus replicates only in the stratum spinosum of the human epidermis, with little or no involvement of the dermis, and does not spread systemically from the site of infection. The host response to infection is progressive and multifactorial. Early in the infection process, interferons, the alternative pathway of complement activation, inflammatory cells, and natural killer cells may contribute to slowing the spread of the infection. The cell-mediated response involving learned cytotoxic T lymphocytes and delayed-type hypersensitivity components appears to be the most important in recovery from infection. A significant role for specific antiviral antibody and antibody-dependent cell-mediated cytotoxicity has yet to be demonstrated in recovery from a primary infection, but these responses are thought to be important in preventing reinfection.

Summary: The cloning and expression of the lux genes from different luminescent bacteria including marine and terrestrial species have led to significant advances in our knowledge of the molecular biology of bacterial bioluminescence. All lux operons have a common gene organization of luxCDAB(F)E, with luxAB coding for luciferase and luxCDE coding for the fatty acid reductase complex responsible for synthesizing fatty aldehydes for the luminescence reaction, whereas significant differences exist in their sequences and properties as well as in the presence of other lux genes (I, R, F, G, and H). Recognition of the regulatory genes as well as diffusible metabolites that control the growth-dependent induction of luminescence (autoinducers) in some species has advanced our understanding of this unique regulatory mechanism in which the autoinducers appear to serve as sensors of the chemical or nutritional environment. The lux genes have now been transferred into a variety of different organisms to generate new luminescent species. Naturally dark bacteria containing the luxCDABE and luxAB genes, respectively, are luminescent or emit light on addition of aldehyde. Fusion of the luxAB genes has also allowed the expression of luciferase under a single promoter in eukaryotic systems. The ability to express the lux genes in a variety of prokaryotic and

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eukaryotic organisms and the ease and sensitivity of the luminescence assay demonstrate the considerable potential of the widespread application of the lux genes as reporters of gene expression and metabolic function.

Summary: The obligately intracellular bacteria of the genus Chlamydia, which is only remotely related to other eubacterial genera, cause many diseases of humans, nonhuman mammals, and birds. Interaction of chlamydiae with host cells in vitro has been studied as a model of infection in natural hosts and as an example of the adaptation of an organism to an unusual environment, the inside of another living cell. Among the novel adaptations made by chlamydiae have been the substitution of disulfide-bond-cross-linked polypeptides for peptidoglycans and the use of host-generated nucleotide triphosphates as sources of metabolic energy. The effect of contact between chlamydiae and host cells in culture varies from no effect at all to rapid destruction of either chlamydiae or host cells. When successful infection occurs, it is usually followed by production of large numbers of progeny and destruction of host cells. However, host cells containing chlamydiae sometimes continue to divide, with or without overt signs of infection, and chlamydiae may persist indefinitely in cell cultures. Some of the many factors that influence the outcome of chlamydia-host cell interaction are kind of chlamydiae, kind of host cells, mode of chlamydial entry, nutritional adequacy of the culture medium, presence of antimicrobial agents, and presence of immune cells and soluble immune factors. General characteristics of chlamydial multiplication in cells of their natural hosts are reproduced in established cell lines, but reproduction in vitro of the subtle differences in chlamydial behavior responsible for the individuality of the different chlamydial diseases will require better in vitro models.